

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claim Status Summary

Claims 1-162 and 164 are requested to be canceled.

Claim 163 is currently being amended.

Claims 165-173 are being added.

Claim Amendments

Claim 163 is amended to correct its dependency to new claim 159.

Claims 165 – 173 are currently being added. Support for claim 165 may be found in the specification, for example at page 30, lines 1-3 and originally presented claim 1 and 159. Support for claim 166 may be found, in the specification, for example, at page 48, Scheme 2. Support for claim 167 may be found in the specification, for example, at page 10, lines 7-8. Support for claim 168 may be found in the specification, for example, at page 10, lines 9-10. Support for claim 169 may be found in the specification, for example, at page 10, lines 11-12. Support for claim 170 may be found in the specification, for example, page 10, lines 13-14. Support for claim 171 may be found in the specification, for example, at page 48, Scheme 2. Support for claims 172 and 173 may be found in the specification, for example, at page 49, Example 2.

Applicants submit that no new matter has been entered by this amendment and respectfully request its entry. Applicants reserve the right to file a continuation or divisional directed to the canceled subject matter.

After amending the claims as set forth above, claims 163, 165-171 are now pending in this application.

Restriction Requirement

Applicants submit that the newly presented claims continue to read on elected Group I. Further, Applicants submit that the newly presented claims continue to read on the elected specie.

Claim Rejections under 35 U.S.C. § 112, first paragraph – Written Description

Claims 159-164 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

In an effort to expedite prosecution, Applicants will apply this rejection to the currently pending claims, namely claims 163, 165-171.

In the Action, it was stated on page 2 of that:

There is insufficient description for the scope as now amended...A careful survey of the specification [finds] description in formula A and analogous compounds, no description of the instant subgenus can be found...

Further, there is no definition for the term radionuclide in terms of elements, size, ionic, or chemical nature of this Markush element. The element finds antecedent basis [for] this term are limited to Rhenium and Technetium...

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116.

Applicants have presented claims directed to a complex containing either a radionuclide of technetium or rhenium and a compound of formula A. There is support in the specification for claims 165 and 172 and the claims dependent therefrom. First, there is specific support for the genus of compounds of formula A as now presented. See, for example, the specification at page 9, line 16 to page 10, line 4. Second, there is support for the use of compounds of Formula A in complexed with a radionuclide. See, for example, the specification at page 30, lines 1-3. Third and finally, as acknowledged in the Action, there is specific support for the radionuclide being either technetium or rhenium. See, for example, the specification at page 30, lines 1-3 and page 49, Example 2.

Support for the dependent claims is outlined above in the section titled “Claim Amendments.”

For the reasons set forth above, Applicants were in possession of the claimed invention at the time of filing. Accordingly, there is ample description for the scope of the currently presented claims and as such, Applicants request withdrawal of this rejection.

Claim Rejections under 35 U.S.C. § 112, second paragraph

Claim 161 stands rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Without addressing the rejection on its merits, Applicants have canceled claim 161 and 162 to expedite prosecution. As such, Applicants request that the rejection be withdrawn.

Claim Rejections under 35 U.S.C. § 112, first paragraph - Enablement

Claims 159-164 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. It is the Office’s position that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to use of the invention commensurate in scope with these claims.

Applicants will apply this rejection to the currently pending claims in an effort to expedite prosecution.

The test of enablement is whether the applicants have taught how to make and use the invention as claimed sufficient to allow one skilled in the art to practice the invention without undue experimentation.

As a matter of Patent Office practice... a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971).

Further, the court in *Marzocchi* has stated, “it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.” MPEP 2164.04; In re Marzocchi, 439 F.2d 220, 169 USPQ 367 (CCPA 1971).

Applicants submit that the Office has failed to meet its burden that the claimed invention.

Without acquiescing to the rejection, Applicants submit that the specification provides sufficient support and teaching of how to make and use the complexes of the invention and as such no undue experimentation is needed to practice the invention. Specifically, Applicants claimed invention is directed to complexes containing a radionuclide of technetium and a compound of Formula A, as well as complexes containing rhenium and a compound of Formula A. The invention is also directed to method of imaging dopamine transporters in brain tissue of a mammal using complexes just described. Applicants have summarized how to make and use the

invention as taught by the specification in the following three points.

First, Applicants respectfully direct the Office to the synthesis of compound 9, a representative compound of Formula A, which can be found on page 7, scheme 1. This synthesis, which begins with readily available starting materials, can be readily adapted by one of skill in the art to make other compounds in Formula A. For example, the specification states that the synthesis is commenced with a piperidine ester, that is readily prepared as reported in the literature. Then, the N₂S₂ chelating group is constructed stepwise.¹ This is the focus of the synthesis of the compounds of the invention. The teaching in this scheme could be readily adapted by one of skill in the art in order to employ other piperidine ester compounds as the starting material. As an aside, claims directed to compounds of Formula A were allowed in the grandparent application and appear in U.S. Patent 6,515,131.

Second, Applicants respectfully direct the Office to the synthesis of the technetium and rhenium complexes, illustrated in the specification. See, for example, page 49, Example 2; page 51, Example 4. Example 2 shows in detail the synthesis of the rhenium-oxo complexes from the N₂S₂ chelating-containing piperidine compounds. This synthesis can be readily adapted by one of skill in the art by substituting the N₂S₂ chelating-containing piperidine compounds. Example 4 shows in detail how to synthesis the radiolabeled technetium-containing compounds. The fact that only a few examples are provided is irrelevant because the specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. In fact, there is no fixed number of compounds which must be named or examples given to provide adequate support for a broad claim, since such number varies, depending on the circumstances of the particular case. In re Shokal et al., 242 F.2d 771, 113 USPQ 283 (CCPA 1957).

Third, Applicants respectfully direct the Office to the specification for how to use the complexes of the invention. Example 5 discusses *in vivo* rat studies of brain uptake of certain

¹ The N₂S₂ chelating group refers to the N,N'-diethylsulfide portion of the molecule.

^{99m}Tc-complexes. Specifically, the studies will evaluate uptake and retention in the brain by sampling tissue at various times following administration of the complexes. The studies will be repeated with β -CIT pretreatment, which competes with dopamine transporter binding, to determine if specific uptake can be blocked. Then a comparison of brain uptake and retention within the series, as well as with other SPECT DAT (single photon emission computed tomography dopamine transporter) complexes, will be performed. See, page 52.

Now, Applicants would like to take the opportunity to address certain statements in the Office Action.

In the Action, page 4, it is stated:

The state of the art in biological imaging material indicated that the particularity of the compound, i.e., its chelating nature and the specific elements carrying radioactivity must form with such particularity in size, charge and stability as to be operable in carrying the emitting material to the site for photon emission topography. There is no evidence in the field that compound with diverse structure or radioelement with diverse size can predict such photon emission tomography requirement. See Kung et al., Cutler et al., or Sohn...

Applicants have obviated this statement, in part, by limiting the claims to complexes with technetium-99m or rhenium. Neither the Sohn nor Cutler et al. references cited by the Office discuss forming complexes with technetium and therefore are irrelevant regarding the enablement of the currently claimed invention. Kung et al., teaches the use of technetium with tropane ligands. Kung et al., however, does not mention piperidine ligands and as such, there is no basis in Kung et al. to support the Office's argument that the current invention is not enabled. The current specification teaches that the complexes of the invention are useful as imaging agents and there is no reason set forth by the Patent Office to support that the complexes would not be useful for this purpose.

The Action also states at Page 4 the following:

In the specification, no definition was given to the size, charge or stability required by the term “radionuclide” with only two elements being exemplified, Re and Tc. The only compound for X is H₂ is compound 9, disclosed on page 7. In addition, compound 9 is a dopamine transporter ligand for which the binding to other anatomical structure of the brain has not been described or supported by the documents of record. The particularity in radiolabeling of the dopamine transporter system finds little generalization that structural diverse compounds or diverse radioactive elements can be operable for such process. Further while binding of dopamine transporter system can provide visual evaluation in diagnosis and monitoring of the disease such as Parkinson’s disease, has not been widely accepted to provide visual evaluation for all possible tissue deviation.

Applicants have obviated this concern as the claims are now directed to a specific radionuclide and the claim directed to methods of imaging brain tissue has been canceled.

Accordingly, Applicants submit that they have provided sufficient guidance to enable persons skilled in the art to make and use the invention as presently claimed. The Officer has not provided any documentation or evidence as to why it doubts the truth or accuracy of Applicants’ assertions in this regard.

In view of the foregoing amendments and remarks, applicants respectfully submit that the instant specification complies with the enablement requirements of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of the objections and rejections thereunder are respectfully requested.

Conclusion

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By Lorna L. Tanner

FOLEY & LARDNER LLP
Customer Number: 38706
Telephone: (650) 251-1104
Facsimile: (650) 856-3710

Lorna L. Tanner
Attorney for Applicants
Registration No. 50,782